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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,420	01/24/2002	Ronald B. Moss	066669-0258	8063

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
08/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/056,420	MOSS ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Serial No.: 10/056,420
Applicants: Moss, R. B., and D. J. Carlo
Filing Date: 01/24/2002

Detailed Office Action

37 C.F.R. § 1.114

A request for continued examination under 37 C.F.R. § 1.114, including the fee set forth in 37 C.F.R. § 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. § 1.114, and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. § 1.114. Applicant's submission filed on 29 May, 2007, has been entered.

Status of the Claims

Claims 1-26 are pending in the instant application.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

As previously set forth, claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. The claims are directed toward a method of treating HIV-infected individuals through structured treatment interruptions (STIs) with immune-based therapies. Antiviral therapy is ceased and patients are immunized with an HIV immunogenic composition that presumably leads to a protective/therapeutic immune response. As previously set forth,

> The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The state-of-the-art as it pertains to HIV-1 and -2 vaccine development is replete with failure. To date, there are no successful HIV-1 or -2 vaccines. The failure to identify and develop suitable vaccines has been due to several factors including: (i) the failure to identify the correlates of protective immunity; (ii) the failure to identify suitable immunogens, adjuvants, routes of administration, and immunization regimens; (iii) the quasispecies nature of lentiviral infection which leads to immune escape, and (iv) the lack of an adequate animal model

that is reasonably predictive of clinical efficacy (Haynes *et al.*, 1996; Lee, 1997; Letvin, 1998; Burton and Moore, 1998; Johnston, 2000; Feinberg and Moore, 2002).

Based upon the proffered exhibits, Applicants appear to have identified a single immunogen (e.g., REMUNE) that appears to provide a positive clinical effect under carefully specified conditions (i.e., selection of patient population, immunization regiment, STI regimen, etc.). However, the identification of a single immunogen in the face of continuing vaccine failure is insufficient to enable the full breadth of the claimed invention.

2) The disclosure fails to provide adequate guidance pertaining to the correlates of protective or therapeutic immunity. In order to assess the true effectiveness of any given immunogen, the skilled artisan would need to know the nature, duration, and specificity of the immune response that confers a salubrious effect on the patient. However, the disclosure fails to provide any guidance pertaining to this subject. Applicants' exhibits and arguments appear to suggest that T_h responses in conjunction with HIV-1-specific CTL responses, under limited circumstances, may provide a clinical benefit. However, none of these parameters appear in the broadest claim language.

3) The disclosure fails to provide adequate guidance pertaining to the preparation of suitable immunogens, adjuvants, routes of administration, and immunization regimens. In order to practice the claimed invention, the skilled artisan would require a knowledge of these parameters. However, the disclosure is silent pertaining to these various parameters. As noted supra, the immunogen REMUNE is the only disclosed immunogen. Considering the previous failures of other HIV immunogens, a single embodiment is insufficient to enable the full breadth of the claimed invention directed toward any sundry immunogenic composition.

4) The disclosure fails to provide any working embodiments. It was

noted that the disclosure provided some preliminary data from a small clinical sample involving the immunogen REMUNE. However, this data cannot be relied upon at this point in time for enablement purposes. It is not readily apparent from reviewing the data that the STI regimen followed by REMUNE immunization was actually providing a therapeutic or protective immune response. The example failed to provide details about the immunological status of each patient participating in the trial. The study failed to measure meaningful immunological and virological indices that would be predictive of vaccine efficacy.

5) The claims are of considerable breadth and encompass any "HIV immunogenic composition." As noted *supra*, there are a number of limitations associated with vaccine development including the identification of suitable immunogens and the correlates of protective immunity. The disclosure fails to provide adequate support for an given HIV immunogen. Applicants' response does not overcome this aspect of the rejection.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Additional Arguments

Applicants submitted several exhibits in the most recent communication which are addressed in more detail as follows:

-Exhibit A: "Guidelines for use of antiretroviral agents" has been considered but the particular relevance of this exhibit is not readily manifest. The examiner is not questioning the guidelines associated with antiretroviral treatment but rather is questioning which immune and virological response in any given study are reasonably predictive of clinical success. For instance, does the patient population require a minimum $CD4^+$ cell count and maximum viral load? After administering any given immunogen, which

parameters are reasonably predictive of a positive clinical outcome?

Exhibit B: The teachings of Moss *et al.* (2003) have been considered. However, this publication is insufficient to enable the full breadth of the claimed invention. First, this study administered a single HIV immunogen, REMUNE. No other suitable HIV immunogens were described. Second, this study demonstrated that REMUNE was only effective after the SECOND STI. Third, there was no indication in this study that the correlates of protection/therapy were generated.

Exhibit C: The teachings of Lichterfeld *et al.* (2004) are also insufficient to overcome the rejection. First, this study also administered a single HIV immunogen, REMUNE. No other suitable HIV immunogens were described. Second, a specific immunization regimen was employed that required at least four doses of the composition. Finally, although generic $CD4^+$ and $CD8^+$ proliferative responses were observed, there was no demonstration that these response were of a high-titer neutralizing nature.

Exhibit D: Fernandez-Cruz *et al.* (2004) reported that under specific conditions statistically significant differences were noted with REMUNE when both the viral load and $CD4^+$ cell count were taken into consideration. Thus, it appears that with patients displaying high viral loads and low $CD4^+$ counts after STI, the immunization/STI regimen will not work. In fact the authors cited another study involving REMUNE (Kahn *et al.*, 2000) wherein positive immune responses were NOT obtained.

Exhibits E and F: Both of these studies employed a specific immunogen (e.g., REMUNE) and specific study conditions which do not appear in the claim language. Accordingly they are insufficient to enable the full breadth of the claim language.

Applicants argue again that the exhibits relied upon would lead the skilled artisan to conclude that the claimed invention is fully enabled. The exhibits appear to demonstrate that a specific composition, designated Remune®, was administered to

patients. This composition comprises gp120-depleted, inactivated HIV-1. However, applicants are reminded that the broadest claim language is directed toward the administration of any "HIV immunogenic composition". While the administration of Remune® appears to be associated with a positive clinical outcome, nevertheless, these findings cannot be extended to other immunogenic compositions because of the unpredictability associated with HIV vaccine development. As previously set forth, the skilled artisan cannot readily predict which immunogens will have a positive clinical outcome. Applicants representative is invited to contact the examiner to arrange for a telephonic interview to further advance prosecution.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey S. Parkin, Ph.D. whose telephone number is 571-272-0908. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

20 August, 2007

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